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Salivary Cortisol: A Psychophysiological Marker for PTSD

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Known as the "stress hormone,"cortisol is secreted at higher levels in the bloodstream during the body's "fight or flight" response to stress as it is responsible for multiple stress related responses in the body. Moderate increases in cortisol levels can have positive effects on the body as energy levels increase, memory functions are heightened, along with the management of homeostasis following a stressful event. However, levels that are too high or too low may have adverse physiological, cognitive and behavioral effects. In previous tests, participants with adverse reactions to stress, often exhibited lower levels of cortisol following a lab-induced trauma-related stressor. Our research is aimed at analyzing the validity of measuring baseline salivary cortisol levels of Soldiers as a marker for individuals who might have PTSD following exposure to combat related stress.

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SALIVARY CORTISOL: A PSYCHOPHYSIOLOGICAL MARKER FOR PTSD

ABSTRACT

Known as the “stress hormone,” cortisol is secreted at higher levels in the bloodstream during the body’s “fight or flight” response to stress as it is responsible for multiple stress related responses in the body. Moderate increases in cortisol levels can have positive effects on the body as energy levels increase, memory functions are heightened, along with the management of homeostasis following a stressful event. However, levels that are too high or too low may have adverse physiological, cognitive and behavioral effects. In previous tests, participants with adverse reactions to stress, often exhibited lower levels of cortisol following a lab-induced trauma-related stressor. Our research is aimed at analyzing the validity of measuring baseline salivary cortisol levels of Soldiers as a marker for individuals who might have PTSD following exposure to combat related stress.

SALIVARY CORTISOL: A PSYCHOPHYSIOLOGICAL MARKER FOR PTSD

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Introduction

This paper focuses on the use of salivary cortisol levels as a tool to predict and diagnose PTSD as well as to assess the effectiveness of the Comprehensive Soldier Fitness (CSF) program. A basic review of stress highlights cortisol's role in the human stress response via its release by the human-pituitary-adrenal (HPA) axis. Research shows that individuals diagnosed with PTSD have generally lower baseline cortisol levels than control groups. However, Soldiers participating in an intervention such as the CSF program may develop resilience and thus have cortisol levels that return to baseline faster following exposure to stress.

History of Combat Stress

With the current military situation in the Middle East, Soldiers are often exposed to stress on a daily basis. This anxiety is often referred to as "combat stress," or the stress that is caused by frequent exposure to combat environments. These stressors can be minimal such as acclimating to a new environment, making daily routine decisions, or the changing deployment/garrison cycles, but most referenced with combat stress are the traumatic events that trigger extreme levels of stress (Bell, et. al., 1997). This exposure to traumatic events often elicits a couple of reactions from humans, one which doesn't seem to effect the psyche (resiliency) and one which leads to a degradation of one's mind, often leading to post traumatic stress disorder (PTSD). However, PTSD is a fairly new concept coined after studying the effects of combat stress. Soldiers of World War I often exhibited a disconnection from one's surrounding following intense artillery bombardment, often associated by the "thousand yard stare." Known as "shell shock," this psychiatric disorder was prevalent in many Soldiers, hampering the combat effectiveness of units in Europe. The degeneration of a Soldier's psyche

continued to be studied following the lesson learned in World War II and Korea. Following the exposure to intense direct combat, many Soldiers exhibited a dysfunctional state characterized as "battle fatigue." Commanders began withdrawing these Soldiers from the front lines into the rear echelons where they could rest and recoup. During the Vietnam War, parallels started to be known between psychological casualties and intense combat, resulting in interest to study what factors lead Soldiers to become a psychological casualty. (Jones, 1995). Post-deployment problems even became evident following the Gulf War in which many veterans exhibit similar symptoms of previous psychological casualties, eventually being coined as "Gulf War Syndrome." A focus of the US military became prevention as psychologists began to develop physical and mental health screening programs aimed at rejecting candidates who exhibited the potential to develop PTSD or PTSD symptoms.

Stress is often known as the negative consequence of the failure to respond appropriately to the emotional or physical threats, no matter if they are real or imagined. This psychological state is often triggered by exposure to events that cause the body to react with symptoms such as elevated heart rate, headaches, irritability, muscular tension, and sometimes the inability to concentrate (Bessel, et. al.,1998). Stress can be caused by the pressures of work, tension of relationships, and many other everyday factors that cause people to experience the anxieties cause by stress. In modern society, stress is believed to have primarily negative effects on human performance, but restricted levels of stress can improve a human's performance as the senses of the body are heightened to the temporary hypervigilance created by the exposure to stress. These healthy levels of stress often cause that feeling of "succeeding under stress" that brings out heightened performance levels (Bower, Moskowitz, & Epel, 2009). An example is athlete performance during a competition or game. The "game time" experience often causes a

sensation in athletes that increase their abilities to a level rarely replicated in practice. However, only certain athletes are actually able to use these heightened levels of stress to their advantage. According to recent polls on ESPN, readers voted shooting two free throws in a National Basketball Association game as the most stressful experience an athlete can face. In these situations, "superstars" are often created. However, even some of the best players in the league who normally average high percentages often succumb to the stress and pressure created by the situation. Here, even professional athletes are negatively affected by heightened levels of stress.

Posttraumatic Growth

With a large portion of training being focused on the development of a Soldier's resilience, another aspect of PTSD and recovery is described as posttraumatic growth (PTG). PTG focuses more on the positive aspects that can result from exposure to trauma as PTG focuses on the positive personal changes that result from an individual's struggle to deal with trauma and its psychological consequences (Tedeschi & Calhoun, 1996). PTG aims at reversing the negative effects of exposure to trauma and is often assessed through an instrument called the Posttraumatic Growth Inventory (PTGI) assessment. The PTGI focuses on renewing the appreciation for life, new possibilities, enhancing personal strength, improving relationships with others, and developing spirituality. Although, any individual is capable of PTG, not everyone necessarily will exhibit PTG.

The Brain & Stress

In addition to understanding the emotional and behavioral aspects of stress, it is also important to understand the physiology in order to manage its effects. When a person thinks a negative event is going to happen they begin to anticipate it. This primary anticipation precipitates an anticipatory emotional response, and this response predicts the physiological changes that will occur during the event itself. According to neuroimaging, stress is associated with activity in the primitive areas of the brain, focusing on the autonomic system and emotional areas located deeper in the brain (Waugh, Tugade, & Frederickson, 2008). The portions of the brain shown to play an important role in the symptoms related to PTSD fall within the limbic system, the insular cortex, the anterior cingulated cortex, the dorsolateral prefrontal cortex, and the orbitofrontal cortex. The insular cortex (IC) is responsible for the regulation of blood pressure and heart rate, along with the autonomic functions of the sympathetic and parasympathetic nervous systems. These systems are both related to the limbic cortex and are connected to the orbitofrontal cortex (OFC) and the amygdala (Nowak et al., 2005; Oppenheimer et al., 1992). These systems are associated with the key responsibilities in relation to the body's reaction to stress. The "fight or flight" response, immune system activation, mobilization of energy, and memory enhancement are common responses of the body to stress, controlled by the autonomic system (Nowak et al., 2005). Heart rate and blood pressure regulation remain important to the mobilization of energy and the amygdala has often been described to be a primary player in the enhancement of memory during exposure to stress or a traumatic event (Southwick et al., 2008).

Another part of the limbic system, the anterior cingulated cortex (ACC), regulates autonomic activity that is responsible for mood changes, emotions, depression, and the

perception of pain. Mood changes, emotional state, and depression are all factors that contribute to the diagnosis of and are common symptoms of PTSD. Many studies have been focusing their efforts on this part of the brain in attempts to prevent the development of PTSD. In a recent study, researchers focused on the effects of pain killers (morphine) and the development of PTSD. The results indicated that for Soldiers who received morphine injections within one hour following a combat related wound, they were 53% less likely to develop or exhibit PTSD symptoms. Heightened during stress, the memory coding responsibility of the limbic system combined with the ACC's role of pain perception would be another relationship to be further studied as they may be a factor in the development of PTSD.

The dorsolateral prefrontal cortex (DLPC) plays a key role in the regulation and encoding of the working memory. One study showed that veterans diagnosed with PTSD had disruptions within their DLPC's following the presentation of both traumatic and non-traumatic images. An additional area of the brain that exhibited increased activity in response to traumatic images was the ventrolateral prefrontal cortex (VLPC), which is associated with emotional control (Cassels, 2009). Therefore, as the activity of the emotional system increases, the cognitive system's performance decreases. This is indicative to the more involved portions of the brain shutting down, which causes a reallocation of cognitive resources to more primitive areas of the brain (responsible for instincts, emotions, and autonomic functions), resulting in decreased response times in reaction to traumatic events (Cassels, 2009).

The orbitofrontal cortex (OFC) is associated with social adjustment and acclimation, along with the control of mood, drive, and responsibility (Cavada & Schultz, 2000). All these responsibilities associated with the OFC are often related to an individual's personality. Change in personality is a common sign exhibited by individuals who are suffering from PTSD. People

close to the PTSD victims often described individuals as distant, and acting unfamiliar to the family to a point atwhich they are viewed as a different person. This parallels with the patient Phineas Gage, who sustained a traumatic brain injury (TBI), losing his personality while experiencing malaise.

Research into the concept of resiliency has received a lot of attention. Resilience is the ability to confront and adapt to stress and adversity (Block & Kremen, 1996). Within in the realm of resilience there are essentially two stages: anticipation and recovery. Anticipation is the emotional or psychological response to an expected or foreseen source of stress. There are three factors that contribute to the anticipatory response to stress: certainty, controllability, and confidence in coping (Waugh, Tugade, & Frederickson, 2008). Recovery is the process by which individuals who have experienced negative effects of stress or adversity gradually and eventually return to their original levels of psychological, functional, and emotional well being. From these two definitions a psychophysiological definition of resilience can be extrapolated: the maintenance of physiological stability such that allostatic load and resulting tissue damage are avoided (Waugh, Tugade, & Frederickson, 2008).

Review of the Metric

As stated before, cortisol is released by the HPA axis during stress response and plays an important role in helping humans respond to stress. Cortisol also plays a vital role in PTSD and resilience. For example, long-term elevated concentrations of cortisol can damage regions of the hippocampus and prevent neurogenesis in the same regions, both of which can interfere with cognition and the future adaptation to stress (Ganzel, Morris, & Wethington, 2010). The majority of studies have found that there is reduced cortisol excretion in victims with PTSD

when compared to the control group (Delahanty et al 2000; Young & Breslau, 2004; Elzinga et al., 2003; Boscarino, 1996).

Several studies in hospitals and clinics show that Vietnam Veterans with PTSD have lower cortisol concentrations in comparison with other veteran psychiatric patients and other studies show that they have lower cortisol levels when compared with healthy control patients (Boscarino, 1996). Further evidence for lower cortisol excretions in PTSD victims is that investigators have reported that male veterans with PTSD have more lymphocyte glucocorticoid receptors than healthy participants (Yehuda, Lowy, Southwick, Shaffer, & Giller, 1991). This is consistent with lower cortistol levels as the body tries to increase reception of the available cortisol in an effort to reach a normal baseline.

Evidence suggests that the physiologic arousal usually observed when a PTSD victim recalls a traumatic event and during the startle response to loud noises is related to alterations in the sympathetic adrenomedullary axis (SAM) and HPA axes of the human stress response (Boscarino, 1996). This suggests a down regulation of the HPA axis in PTSD (Delahanty et al., 2000). More specifically, PTSD results in chronically lowered levels of corticotropin releasing hormone (CRH), which is needed to release cortisol (Boscarino, 1996). The mechanism that causes this down regulation and characterizes PTSD is a heightened sensitivity of the glucocorticoid negative feedback loop at the pituitary (Delahanty et al., 2000). In other words, PTSD victims suffer from hyper-vigilance and recurring intrusive thoughts. These cause their stress response to be over activated due to the perception of threat which, in turn, cause their cortisol levels to be elevated for an extended period of time. The negative feedback loop is activated and the body stops producing cortisol via a lowering in CRH production. This leads to a lower baseline level of cortisol in the human body.

Kardiner (1941) used the term "physioneurosis" to describe PTSD. He made note of the fact that while victims cope with their environments by emotional constriction, their bodies continue to behave to specific physical and emotional stimuli as if there were still a continuing threat of destruction. Beginning with studies by Dobbs and Wilson (1960), there was note of conditioned autonomic arousal to combat stimuli which has been repeatedly documented in veterans with PTSD. Many researchers have found that there are significant conditioned reactions in response to stimuli that is akin to the original trauma, as measured by heart rate, blood pressure, and electromyogram (Van der Kolk & Saporta, 1991).

A hypothesis linking autonomic arousal and intrusive recollections has been around for a long time and there is research that supports this link. Rainey et al. (1987) showed that the administration of lactate, which stimulates physiological arousal, produced PTSD-like flashbacks in 7 out of 7 subjects and panic attacks in 6 out of 7 patients with PTSD. Southwick et al. (1989) were able to produce somatosensory flashbacks in people with PTSD by injecting yohimbine into participants. The yohimbine stimulates norepinephrine release in the locus coeruleus. These studies suggest a biological link to flashbacks, panic, and PTSD.

A higher order psychological explanation of this can be found in behaviorism. Those exposed to traumatic stressors, which it is suggested acts as unconditioned aversive stimuli, evoke severe autonomic physiological distress. As a result, previously neutral external stimuli (e.g., aspects of the physical environment) and internal stimuli (e.g., physiological states, emotions, and cognitions) that accompanied the traumatic stressor, may function as conditioned stimuli capable of producing significant psychological and physiological distress even when the traumatic stressors are no longer present (Boscarino, 1996).

This would suggest that people would not only try to avoid the unconditioned stimuli (i.e., the traumatic stressor), but also try to engage in behaviors that they feel are necessary to avoid aversively conditioned external and internal stimuli indirectly associated with it. This avoidance of averse conditioned stimuli may be reinforced with aversive arousal reduction (i.e., negative reinforcement). This could function to encourage avoidance in the future and, while it may produce a temporary reduction in aversive arousal, it may also prevent the extinction that would occur over time. This then contributes to the chronicity seen with PTSD (Boscarino, 1996). Additionally, this explains the constant peaking of cortisol levels in the body that eventually lead to a lower production of the hormone and, thus, a lower cortisol baseline.

Another cognitive explanation behind the chronicity of PTSD lies in schemas. People hold certain assumptions, or schemas, about the world and the self. Once a schema is formed there is a strong tendency to hold that schema as true. In the event that information in the world doesn't match the schema people tend to assimilate the information into the schema instead of change the schema to match the new information (Anderson & Lindsay, 1998).

However, traumatic events undermine this tendency. Traumatic events are unpredictable, uncontrollable, and negative, all of which lead to activation of the HPA axis (threat oriented) and the production of cortisol. Traumatic events usually shatter the schema of invulnerability that most people posses and contradict their positive world view. The intensity and vividness of the traumatic experience prevent people from ignoring the new information or assimilating this new information into established schemas and leaves them with an accommodated negative world view (Ginzburg, 2004).

This negative world view can lead to pessimism which reinforces the sense of threat by confirming the dangers of the world and by preventing the individual from assimilating new,

more positive, and calming information that would allow him or her to change the negative world view. This constant state of perceived threat leads to the continued activation of the HPA axis and high cortisol production (Ginzburg, 2004). It is evident that cortisol is an important factor in PTSD that warrants further study.

Past Uses and Findings

Traditionally, cortisol levels are taken in the task of diagnosing Cushing's syndrome which is a hormonal irregularity (Papanicolaou et al., 2002). However, there is a growing body of work done with cortisol in the field of PTSD. Boscarino (1996) conducted a study comparing morning serum cortisol levels among a national sample of Vietnam "theater" veterans (n=2,490) and a sample of Vietnam "era" veterans (n=1,972) without service in Southeast Asia. Analysis of covariance was used after adjusting for 9 covariants of education, income, race, age, smoking status, alcohol use, illicit drug use, medication use, and body mass index. This study found that adjusted cortisol was lower among theater veterans with current PTSD with cortisol concentrations inversely proportional to combat exposure (the heavier the combat, the lower the levels of cortisol).

Delahanty et al. (2000) conducted a study designed to examine the relationship between urinary hormone levels collected upon admission to the trauma unit following a motor vehicle accident and PTSD symptomatology 1 month later. They used fifteen-hour urine samples from 63 male and 36 female motor vehicle accident victims and assessed levels of catecholamines and cortisol reflecting peritraumatic and acute-phase posttraumatic levels. They found that victims subsequently diagnosed with PTSD had significantly lower levels of urinary cortisol upon admission to the hospital. Additionally, urinary levels of cortisol predicted a significant percentage of the variance in intrusive and avoidant thoughts 1 month after the accident.

Alpers et al. (2003) sought to determine if the HPA axis is activated by phobic anxiety. Salivary cortisol was measured in 11 driving phobics before and during three exposure sessions involving driving on crowded, limited-access highways. They were compared with 13 healthy controls before and during driving. The results indicated that the phobics levels of cortisol were higher than the controls during treatment and concluded that the HPA axis is very much triggered by exposure to and anticipation of phobic situations. The main thing we garnered from this study was the paradigm used to collect and evaluate salivary cortisol. However, this article also demonstrates that there is stimulus specificity to autonomic hyper-arousal. There was some doubt as to whether or not autonomic hyper-arousal could be attributed to one stimulus alone, but this study suggests that it very well could be.

Young and Breslau (2003) conducted an experiment to study the relationship between cortisol and catecholamine levels in PTSD victims. They used urine samples from a cohort of young adults assessed periodically during a 10 year period for exposure to trauma and PTSD. From that group a subset (n=913) was selected for urine analysis conducted in a sleep lab across 2 consecutive nights and the intermediate day. The criteria for the subset were (1) exposed to trauma during the preceding 5 years, (2) others who met PTSD requirements, and (3) random preselected sample. There were 439 eligible individuals, 292 participated, including 69 with lifetime PTSD. They found that while catecholamine levels were higher in persons with PTSD and those exposed to trauma without PTSD, cortisol levels remained constant across the groups. This could be because they took urine samples in 4 groups, each covering 8 hours. Urinary cortisol experiments typically collect all urine for a 24 hour period in one bag to get an accurate assessment of cortisol during the full circadian rhythm as cortisol levels decrease and increase during a 24 hour period and are variable from day to day.

Rationale for Proposed Study Method

We chose to use salivary cortisol as our metric to assess PTSD. We chose cortisol because of its key role in the human stress response and the ease with which it can be collected. We specifically chose salivary cortisol because of its accuracy and non-invasiveness. Papanicolaou et al. (2002) did a study comparing salivary, urinary, and plasma cortisol collection methods in the diagnosis of Cushing's syndrome. Up to 30% of urine cortisol may return an incorrect result which suggests a need for a better test. They evaluated the utility of nighttime salivary coritsol measurement as a screening test for Cushing's syndrome. They evaluated 139 inpatients and 4 outpatients with possible Cushing's syndrome, 16 inpatients and 7 outpatients with other nonadrenal disorders, and 34 healthy outpatients. They used cut points to exclude all subjects without Cushing's syndrome. They compared the sensitivity for detection of nighttime salivary cortisol levels (2330 and 2400 hours for inpatients and bed time for outpatients), simultaneous inpatient serum cortisol levels, and urine glucocoritcoid excretion. They concluded that salivary cortisol measurements worked as well as plasma measurements and better than urine cortisol excretion. Salivary cortisol identified more than 90% of patients with the disorder.

Salivary cortisol offers a number of advantages: it reflects the unbound fraction of circulating cortisol and is, therefore, unaffected by changes in cortisol binding globulin (found in oral contraceptives). Salivary cortisol is not influenced by saliva flow rate and there are obvious advantages to collection at home at bedtime: there is no need for an office visit and the risk of a rise in cortisol levels from anxiety from unfamiliar surroundings is reduced. However, they recommended that participants refrain from eating or physical activity for 3 hours before collection (Papanicolaou et al., 2002).

Proposed Study Method

Baseline

Another advantage of cortisol is that, in theory, it could be used to predict PTSD, diagnose PTSD, and assess any treatment that a patient receives. However, for all of these a baseline cortisol level would need to be established. We would use a salivette to collect the sample and the method we would use to establish this level is as follows:

- Participants told to avoid exercise, eating, or drinking 3 hours before collection
- Participants chew on salivette for 45-60 seconds
- Participants will keep salivettes in refrigerator until they report to the medical clinic where they will be frozen in the facility's freezer
- Participants will produce another sample 30 minutes before lunch and deliver it to the medical clinic where it will be frozen in the facility's freezer
- Participants will produce another sample immediately before bed ,but no sooner than 3 hours after exercise, eating, or drinking and will refrigerate this sample until the next morning when they take it to the medical clinic
- This process will continue for a week
- The samples can then be sent to an independent lab for analysis or use a direct, nonextraction assay kit (Coat-a-Count kit; Diagnostic Products Corporation, Los Angeles, CA)

Salivettes should be frozen when possible, but they can be stored at room temperature for up to a week without a significant reduction in cortisol levels (Houtveen & de Geus, 2009).

Prediction

For the prediction paradigm we will use one similar to the paradigm used in Alpers et al. (2003) driving phobia experiment. The goal here is to determine how quickly the participants' cortisol level returns to baseline; the faster the return to baseline the more resilient they are.

- Participants will be instructed not to eat, drink, or conduct physical activity 3 hours prior to collection
- Saliva will be collected immediately after awakening (before brushing teeth) the day of the stressor application
- Saliva will be collected one hour before the stressor is applied
- Immediately after the first saliva collection participants will take an anxiety test
- Saliva will then be collected again immediately after the application of the stressor
- Saliva samples will then be collected every hour on the hour for three hours after the stressor is applied to gauge speed of recovery; at each collection participants will take an anxiety test. There is a need to collect samples throughout the day because cortisol levels change throughout the day, peaking in the morning around 0600 hours and reaching a low around 2200 hours. There is also a need to test throughout the week because cortisol levels vary from day to day and we want to make sure the baseline profile is as accurate as possible.
- Samples can then be sent to a lab to be tested for cortisol levels or they can be tested by the experimenter with an ambulatory test kit

Diagnosis

In the diagnoses paradigm we would only need to test the participants' baseline level of cortisol. This would be done in the same way as outlined above in the "Method" section except samples would be collected only at 0800 and 2000 hours. Normal salivary cortisol levels for an adult are: 15.5 +/- .8 nmol/L at 0800 hours and 3.9 +/- .2 nmol/L at 2000 hours (Laudat et al., 1988). Participants would also take the Posttraumatic Cognitions Inventory to test for PTSD (Foa et al., 1999). The participant's medical records would also be accessed for any indication of PTSD. Analysis would be run on the results to see if the samples are significantly lower than the proposed normal levels. If they are and the participant scored positive for PTSD on the PTCI then it would be suggested that the participant has PTSD.

Assessment

Cortisol can also be used to assess the effectiveness of the CSF training. This would be a "before and after" paradigm. Baseline levels would be recorded in accordance with the paradigm outlined in the "Method" section of this paper and samples would be taken during the week leading up to the training. After completion of the training saliva samples would be taken again for another week. The two samples would then be analyzed using to see if there was an increase in baseline cortisol levels and then analyzed to see if that increase was significant. What we would expect to see would not only be an increase in baseline cortisol levels but a significant one, close to or at the normal levels outlined in the previous section.

SWOT Analysis: *Strengths, Weaknesses, Opportunities, and Threats*

One of the strengths of this proposed method is its ability to provide quantitative objective data supported by previous research. Cortisol levels are significantly linked to PTSD

and our method provides an assessment tool for prediction, diagnoses, and assessment of treatment. Another strength is that salivary cortisol collection is fairly unobtrusive (expectorate in salivettes). It only requires that participants chew on a cotton swab for approximately a minute. A third strength is that there is the large participant pool from which to draw upon. The participants will be active duty U.S. Army Soldiers who belong to brigade combat teams.

The main weakness of this method is that there is no specific cortisol profile for PTSD victims. We know that cortisol levels are lower in patients with PTSD but there are no data available to say that there is a specific level of cortisol associated with PTSD. We must rely on statistics to analyze if the drop from normal baseline is a significant one. This could lead to misinterpretation of the data if a person has a low baseline of cortisol due to genetics or some external factor. Thus, it is important to include subjective psychological measures to supplement the cortisol measurement.

There are several opportunities that allow this method to be successful. There is a large pool of available participants. We plan to use 8 Brigade Combat Teams, each of which consist of about 3,500 Soldiers each. Also, there will be participants with varying levels of disease (no symptoms to catastrophic symptoms) so we will have the full spectrum of Soldiers to test. This will give our study external validity because all three methods (prediction, diagnoses, and assessment) can be tested within the same test group.

There are several threats that can affect this study. Food and exercise can affect cortisol levels. Any stress on the body can make cortisol levels rise which is why it is important that participants adhere to the 3 hour rule. This leads us to our next threat; participant reliability. Since the participants can collect their own samples at home there is no way to track that they are following correct procedures. There are also threats from medication. Medications such as

gluccocorticoids, lithium, diuretics, estrogen and tricyclic antidepressants can interfere with cortisol levels. It is important that patients taking these medications be identified and excluded from the study. As stated before, salivary cortisol is not affected by oral contraceptives so women taking birth control pills can still participate in the study.

Summary

Salivary cortisol is an effective, accurate, and efficient means to collect data on PTSD. Cortisol is a key hormone in the human stress response that may aid in predicting resilience, diagnosing PTSD, and assessing treatment or program effectiveness. It may play a key role in not only assessing the effectiveness of the Comprehensive Soldier Fitness program but also has many other applications. The possibilities that exist with cortisol could lead to a way to not only predict resilience but also a simple way to objectively diagnose someone with PTSD. Future research should focus on establishing a cortisol baseline profile for a victim of PTSD. To make it a true diagnostic we would need some sort of threshold that said, "At this point you have PTSD". The expectation would be to create a scale that said, "If you're baseline level of cortisol is this, then your PTSD is this severe." Cortisol levels may also be recorded in conjunction with other physiological measures such as heart rate and neuropeptide Y to provide a more complete profile of resilience and PTSD.

Annotated References

Alpers, G. W., Abelson, J. L., Wilhelm, F. H., & Roth, W. T. (2003). Salivary cortisol response during exposure treatment in driving phobics. *Psychosomatic Medicine, 65,* 679-687.

This article provided us with a method to collect saliva samples. It also provided evidence that suggests that the HPA axis can be triggered by a single stimulus.

Anderson, C.A., & Lindsay, J. J. (1998). The development, perseverance, and change of naïve theories. *Social Cognition, 16,* 8-30.

This article talked about schemas and how they relate to a person's world view. It also talked about how people cope with information that does not match their schema.

Bell, D.B., Bartone, J., Bartone, P.T., Schumm, W.R., & Gade, P. A. (1997). *USAREUR family support during Operation Joint Endeavor: Summary report* (ARI Special Rep. No. 34). Alexandria, VA: U.S. Army Research Institute for the Behavioral and Social Sciences.

The report focused on combat stress and the contributing factors that create many of the negative symptoms of PTSD.

Bessel, A., Van der Kolk, McFarlane, A., & Weisaeth, L. (1998). The effects of overwhelming experience on mind, body, and society. *Traumatic Stress* (pp. 117-242). New York City: The Guilford Press.

This book was composed of multiple chapters focused on how the mind and body are related when experiencing various forms of combat stress. The chapter utilized focused on combat stress and the effects from that on developing PTSD.

Block, J. & Kremen, A. M. (1996). IQ and ego-resiliency: Conceptual and empirical connections and separateness. *Journal of Personality and Social Psychology*, 70(2), 349-361.

The article analyzed the relationship between stress and resiliency.

Boscarino, J. (1996). Posttraumatic Stress Disorder, Exposure to Combat, and Lower Plasma Cortisol Among Vietnam Veterans: Findings and Clinical Implications. *Journal of Consulting and Clinical Psychology, 64,* 191-201.

This article focuses on plasma cortisol levels in Vietnam veterans and reviews cortisol's role in PTSD. The article suggests that PTSD victims have lower cortisol levels than control groups.

Bower, J. E., Moskowitz, J. T., Epel, E. (2009). Is benefit finding good for your health?: Pathways linking positive life changes after stress and physical health outcomes. *Current Directions in Psychological Science* 18: 337-341.

The article discusses how there are positive correlations between appropriate levels of stress and how it can help humans perform at higher levels.

Cassels, C. (2009). Brains of veterans with and without PTSD differ, imaging study shows. *J Psychiatr Res. 43*(8), 809-17.

This article examines the functioning of the dorsolateral and ventrolateral prefrontal cortexes and their role within PTSD.

Cavada, C. & Schultz, W. (2000). "The Mysterious Orbitofrontal Cortex". *Cerebral Cortex.* 10(3), 205.

Provides an overview of the OFC and its relationship to a variety of behaviors such as PTSD, decision-making and compulsive behaviors.

Delahanty, D.L., Raimonde, A. J., & Spoonster, E. (2000). Initial posttraumtatic urinary cortisol levels predict subsequent PTSD symptoms in motor vehicle accident victims. *Society of Biological Psychiatry, 48*, 940-947.

This study was designed to examine the relationship between urinary hormone levels after motor vehicle accidents and PTSD. The authors found that participants diagnosed with PTSD secreted lower levels of cortisol than control groups.

Dobbs, D., & Wilson, W. P. (1960). Observations on the persistence of traumatic war neurosis. *Journal of Mental & Nervous Disease, 21*, 40-46.

This article explained conditioned autonomic arousal to combat stimuli which has been repeatedly documented in veterans with PTSD and helps explain the chronicity of PTSD.

Elzinga, B.M., Schmahl, C. G., Vermetten, E., van Dyck, R., Bremner, J.D. (2003). Higher cortisol levels following exposure to traumatic reminders in abuse-related PTSD. *Neuropsychopharmacology, 28,* 1656-1665.

The authors provide an explanation for lower cortisol levels in PTSD victims. There are lower cortisol levels because there is a continually high level of cortisol in people with PTSD so the body compensates by producing less cortisol so the baseline level is lower.

Foa, E. B., Ehlers, A., Clark, D. M., Tolin, D.F., Orsillo, S.M. (1999). The Posttraumatic Cognitions Inventory (PTCI): Development and validation. *Psychological Assessment, 11*, 303-314.

This article describes the development and validation of a new measure of trauma-related thoughts and beliefs. The PTCI's items were developed from clinical observation.

Ganzel, B.L., Morris, P. A., & Wethington, E. (2010). Allostasis and the human brain: Integrating models of stress from the social and life sciences. *Psychological Review, 117,* 134-174.

This article suggests that constantly high levels of cortisol can damage areas of the hippocampus. The damage caused by the cortisol then causes a lack of ability to cope with stress in the future. This article also provides an overview of the theory of allostasis.

Ginzburg, Karni (2004). PTSD and world assumptions following myocardial infarction: A longitudinal study. *American Journal of Orthopsychiatry, 74,* 286-292.

This study aims to examine the association between exposure to trauma, PTSD, and world assumptions. The findings suggest that world assumptions are associated with PTSD.

Houtveen, J. H. & de Geus, E. J. C. (2009). Noninvasive psychophysiological ambulatory recordings: Study design and data analysis strategies. *European Psychologist, 14,* 132-141.

This article reviews different mobile ways of collecting and analyzing biometric data. We used this article to help develop our methods section.

Jones, F.D. (1995). Psychiatric lessons of war. In In R. Zajtchuk, R.F. Bellamy & Jenkins, D.P. (Eds.), *War Psychiatry* (pp. 3-33). Washington, DC: TMM Publications.

This textbook includes a history of war-related trauma and the physical, behavioral and physiological effects associated with combat to include: disfigurement, PTSD, conversion disorders and traumatic brain injury.

Kardiner, A. (1941). *The traumatic neuroses of war.* New York: Hoeber.

This article describes the behavior of PTSD victims. It explains how they mentally cope with their ordeal but their bodies still react to emotional and physical stimuli as if a threat still exists.

Laudat, M.H., Cerdas, S., Fournier, C., Guiban, D., Guilhaurne, B., & Luton, J.P. (1988). Salivary cortisol measurement: a practical approach to assess pituitary-adrenal function. *Journal of Clinical Endocrinology and Metabolism, 66,* 343-348.

This article established a normal baseline level of cortisol. We use this baseline as our comparison when analyzing participants for PTSD in our diagnosis section.

Nowak M., Holm S., Biering-Sørensen F., Secher N.H., & Friberg L. (2005). Central command and insular activation during attempted foot lifting in paraplegic humans. *Human Brain Mapping*, *25* (2): 259–65.

This article was utilized to determine the role of the insular cortex in relation with the limbic system, the orbitofrontal cortex, and stress management.

Oppenheimer S.M., Gelb A., Girvin J.P., Hachinski V.C. (1992). Cardiovascular effects of human insular cortex stimulation. *Neurology, 42* (9): 1727–32.

This article was utilized to determine the role of the insular cortex in relation with the limbic system, the orbitofrontal cortex, and stress management.

Papanicolaou, D. A., Mullen, N., Kyrou, I., & Nieman, L. K. (2002). Nighttime salivary cortisol: A useful test for the diagnosis of Cushing's Syndrome. *The Journal of Clinical Endocrinology and Metabolism, 87*(10), 4515-4521.

This article establishes that salivary cortisol is just as accurate as serum cortisol and is more accurate than urinary cortisol measurements. It provides validation for using salivary cortisol over the other two methods.

Rainey, J.M., Aleem, A., Ortiz, A., Yaragani, V., Pohl, R. & Berchow, R. (1987). Laboratory procedure for the inducement of flashbacks. *American Journal of Psychiatry, 144,* 1317-1319.

This study showed that the administration of lactate could produce PTSD-like flashbacks. This provides evidence that there is a relationship between autonomic arousal and intrusive thoughts.

Southwick, S., Morgan, C.A., Charney, D.S., & High, J.R. (1989). Yohimbine use in a natural setting: Effects on posttraumatic stress disorder. *Biological Psychiatry, 46*(3), 442-444.

This article provides evidence that suggests that there is a relationship between autonomic arousal and intrusive thought. The researchers injected yohimbine into participants which cause norepinephrine to be released in the locus coeruleus and induced somatosensory flashbacks.

Southwick, S., Ozbay, F., Charney, D., & McEwen, B. (2008). Adaptation to stress and psychobiological mechanisms of resilience. In B. J. Lukey & V. Tepe (Eds.), *Biobehavioral Resilience to Stress* (pp. 91-108). Boca Raton: CRC Press.

This chapter focused on the aspects of stress and resilience. It provided an in-depth analysis of resilience and recent methods developed to enhance it.

Tedeschi, R. G., & Calhoun, L. G. (1996). The Posttraumatic Growth Inventory: Measuring the positive legacy of trauma. *Journal of Traumatic Stress, 9*, 455-471.

This study describes the development of the Posttraumatic Growth Inventory. The PTGI is used to assess positive outcomes that are reported by persons who have experienced traumatic events in 5 main factors: New Possibilities, Personal Strength, Spiritual Change, and Appreciation of Life.

Van Der Kolk, B. & Saporta, J. (1991). The biological response to psychic trauma: Mechanisms and treatment of intrusion and numbing. *Anxiety Research, 4*, 199-212.

This article reviews the human stress response and provides several explanations for PTSD, both biological and psychological. We used it to establish the link between psychology and biology.

Waugh, C., Tugade, M., & Fredrickson, B. (2008). Psychophysiology of resilience to stress. In B. J. Lukey & V. Tepe (Eds.), *Biobehavioral Resilience to Stress* (pp. 117-134). Boca Raton: CRC Press.

This chapter focused on the physiology and brain structures connected with resilience and stress.

Yehuda, R., Lowy, M. T., Southwick, S. M., Shaffer, D., & Giller, E. L. (1991). Lymphocyte glucocorticoid receptor number in posttraumatic stress disorder. *American Journal of Psychiatry, 148,* 499-504.

This article showed that there was a higher number of glucocorticoid receptors in people with PTSD than in people without it. This suggests that there is a change in the HPA axis in people with PTSD.

Young, E.A. & Breslau, N. (2004). Cortisol and catecholamines in posttraumatic stress disorder: An epidemiologic community study. *Arch Gen Psychiatry, 61,* 394-401.

The purpose of this article was to examine urinary catecholamine and cortisol levels in people with PTSD in a community sample. They found that cortisol levels did not differ between groups while catecholamine levels did.